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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,094	03/08/2001	Paul Calabresi	21486-038	4935

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 01/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/802,094

Applicant(s)

CALABRESI ET AL.

Examiner

Christopher H Yaen

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 September 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 9, 12-15 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 9, 12-15 and 17-20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet.  
37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. The amendment filed 9/26/2003 is acknowledged and entered into the record. Accordingly, claims 1-8, 10-11, and 16 are cancelled without prejudice or disclaimer.
2. Claims 9, 12-15, and 17-20 are pending and examined on the merits.

#### ***Claim Rejections Maintained - 35 USC § 103***

The rejection of claims 9, 12-15, and 17-20 under 35 USC 103(a) as being obvious over Joshi *et al* in view of O'Leary, Sheibani and Streit is maintained for the reasons of record. Applicant argues that the amendments to the claims to reflect a TSP polypeptide renders the claim free of the prior art, and that Joshi *et al* does not specifically teach the administration of a polypeptide, but instead discloses the administration of a nucleic acid molecule. Applicant's arguments have been carefully considered but are not found persuasive. Joshi *et al* teaches the combination of using TSP and DNA topoisomerase inhibitors in the treatment of cancer (see for example page 15). Although Joshi *et al* teaches the combination of using genes and DNA topoisomerase inhibitors, one of ordinary skill in the art would have found it obvious to use polypeptides in place of the nucleic acid molecules both Sheibani *et al* and Streit *et al* taught that the protein form of TSP was effective in treating angiogenic conditions in vivo. Furthermore, O'Leary *et al* taught that the combination of an angiogenic inhibitor in combination with camptothecin, a DNA topoisomerase inhibitor, was effective in initiating an anti-tumor response. Therefore, one of ordinary skill in the art would have found it obvious to use a peptide or polypeptide in place of nucleic acids to initiate an

anti-tumor response because Joshi *et al* taught the initial combination of products (i.e TSP and DNA topoisomerase inhibitors), that Sheibani *et al* and Streit *et al* taught that TSP polypeptides are effective in treating angiogenesis in an *in vivo* model, and that the combination of anti-angiogenic compounds and camptothecin are effective in initiating an anti-tumor response. One of skill would have expected a reasonable amount of success in doing so because it was already well established that TSP was an effective endogenous anti-angiogenic compound and that topoisomerase inhibitory compounds such as camptothecin were effective as anti-cancer agents via mechanisms of inhibiting angiogenesis, as evidenced by O'Leary *et al*. Therefore, because both TSP and DNA topoisomerase inhibitors such as camptothecin, are effective on their own in inhibiting tumor cell growth, as set forth in *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980), "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose...the idea of combining them flows logically from their having been individually taught in prior art".

### ***New Arguments***

#### ***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 9,12,17-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Thorpe *et al* (US Patent 6,406,693). Claims are drawn to a method of inhibiting tumor cell growth in a mammal, comprising administering to said mammal a composition comprising a TSP polypeptide and an inhibitor of DNA topoisomerase I enzyme activity, wherein said tumor cell is a colon tumor cell, wherein said TSP polypeptide is TSP-1 or TSP-2 and said inhibitor of DNA topoisomerase I enzyme activity is a water soluble camptothecin compound, and wherein tumor growth is inhibited in the presence of said TSP polypeptide and said water soluble camptothecin compound compared to in the absence of said TSP polypeptide and said water soluble camptothecin compound (claim 9). The claims are further limited to the TSP being TSP-1 (claim 12), the mammal being human (claim 17), the administration of the TSP polypeptide prior to (claim 18), after (claim 19), or simultaneously (claim 20) with DNA topoisomerase inhibitor.

Thorpe *et al* disclose a method of treating colon cancer in a human with a composition which comprises camptothecin (see column 72) and a TSP, specifically TSP-1 (column 79). Thorpe *et al* also disclose that the administration of the compounds can be done so according to the claimed regimen of claims 18-20, wherein there are compounds administered prior to, after or simultaneously (column 19).

### **Conclusion**

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen  
Art Unit 1642  
December 24, 2003

  
CHRYSTOPHER Y. YAEN, EXAMINER  
ART UNIT 1642